UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,355	07/12/2005	Vicki S Elliott	071949-9301	6312

22428 7590 01/22/2008

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
CARLSON, KAREN C	
ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
01/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,355	ELLIOTT ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *140 and 144-157* is/are pending in the application.

4a) Of the above claim(s) *147-156* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *140, 144-146, 147* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office Action is in response to the paper filed November 9, 2007.

Claims 1-139 and 141-143 have been cancelled. Claims 140 and 144-157 are currently pending. The Examiner has withdrawn Claims 147-156 from further consideration because these claims are drawn to non-elected inventions. Claims 140, 144-146, and 157 are currently under examination.

Benefit of priority is to provisional application 60/410566, filed September 13, 2002, wherein instant SEQ ID NO: 11 is taught as SEQ ID NO: 3 therein.

Withdrawal of Objections and Rejections:

The rejection of Claims 140-146 and 157 under 35 U.S.C. 112, second paragraph, is withdrawn.

The rejection of Claims 140, 142, 144, 145,146 and 157 are rejected under 35 U.S.C. 102(b) as being anticipated by Morser et al. (USP 5,864,018) is withdrawn in response to the amendments of the claims.

Maintenance of Objections and Rejections:

The substitute specification filed November 9, 2007 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because: the filing of a substitute specification is to clean up minor errors in the original specification. Issues of new matter by deletion of all of this information arises, it is not clear if this national stage application is still considered a 371 of the PCT because it is now effectively a CIP of the PCT, and the oath and declaration may have to

be re-submitted. Further, if Applicants intend to file DIVs for other CADECMs, they would have no basis in this substitute specification and issues of priority would arise.

Please return the specification to the original, with amendments to clean up minor errors.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 140, 144-146, and 157 are again rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, credible, asserted utility or a well established utility.

The specification is silent regarding the activity of SEQ ID NO: 11. In Table 2 at page 113, SEQ ID NO: 11 is annotated as being related to the receptor for advanced glycation end products (RAGE). However, no where in the specification is there a positive recitation that SEQ ID NO: 11 is expected to have activities associated with RAGE is set forth.

Numerous alternative splice variants of RAGE are known in the art. Those skilled in the art of RAGE splice variants recognize that the splice variants have different functions from RAGE, and even different functions between themselves. The Examiner cites the following references as evidence that splice variants of RAGE are considered to have different structure and function from wild-type RAGE:

Hudson et al. (2006a; Lentivirus gene transfer of the endogenous circulating RAGE splice form blocks mechanisms leading to atherosclerosis. Circulation 114(18 Suppl. S): 25-26) teach alternatively spliced RAGE resulting from the inclusion of introns 9 (RAGEint9). RAGEint9 reduced S100B stimulated MMP-9 activity and reduced IL-6 when compared to wild-type RAGE. Hudson et al. conclude that RAGEint9 is a novel therapeutic modality to enhance protection against artherosclerotic disease associated with RAGE.

Hudson et al. (2005; A novel method for the detailed analusis of gene splice variants. FASEB J. 19 (4, Supple. S, Part 1): A855) teach numerous splice variants of RAGE and conclude that these variants change the structure and function of RAGE because they altered the ligand binding domain, extensively removed the extracellular domain, and produced soluble RAGE lacking the transmembrane domain. See also Hudson et al. (2006b; Alternative splicing of the RAGE gene: Analysis and characterization in humans and mice. FASEB J. 20 (5, part 2) A1081).

Schlueter et al. (2003; Tissue-specific expression patterns of the RAGe receptor and its soluble forms – a result of regulated alternaive splicing? Biochimica et Biophysica Acta 1630: 1-6) teach soluble RAGE lacking the transmembrane and cytoplasmic domains that is an inhibitor of RAGE.

Harashima et al. (2006; Identifiction of mouse orthologue of endogenous secretory receptor for advanced glycation end-products: structure, function and expression. Biochem. J. 396:109-115) teach endogenous secretory RAGE (esRAGE) that is a decoy receptor for RAGE and protects cells and tissues from ligand-dependent injury such as early retinal complications from diabetes.

Park et al. (2004; Expression of a novel secreted splice variant of the recpetor for advanced glycation end products (RAGE) in human brain astrocytes and peripheral blood mononuclear cells. Molecular Immunology 40: 1203-1211) teach splice variant of RAGE lacking exon 8 and conclude that the diverse expression of RAGE isoforms modify RAGE mediated pathogenesis.

From this survey of the literature, it is evident that SEQ ID NO: 11 is a splice variant of RAGE. The specification does not positively recite a function for SEQ ID NO: 11, and those skilled in the art would not expect this splice variant of SEQ ID NO: 11 to have the same function as RAGE. Therefore, the claimed invention does not have a specific, substantial, credible, asserted utility or a well-established utility.

Applicants urge that RAGE has been taught in the prior art to be useful in treating diabetes. The specification at page 62, line 15 discloses to use the polypeptide in the treatment of diabetes mellitus. Applicants conclude that the claimed invention has utility.

Perusal of page 62 in the specification filed 2/14/2001, which was not entered but does recite diabetes mellitus at line 15, states:

Therefore, in one embodiment, CADECM or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of CADECM. Examples of such disorders include, but are not limited to, an immune system disorder, such as acquired immunodeficiency syndrome (AIDS), X-linked agammaglobinemia of Bruton, common variable immunodeficiency (CVI), DiGeorge=s syndrome (thymic hypoplasia), thymic dysplasia, isolated IgA deficiency, severe combined immunodeficiency disease (SCID), immunodeficiency with thrombocytopenia and eczema (Wiskott-Aldrich syndrome), Chediak-Higashi syndrome, chronic granulomatous diseases, hereditary angioneurotic edema, immunodeficiency associated with Cushing=s disease, Addison=s disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), bronchitis, cholecystitis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, **diabetes mellitus**, emphysema, episodic lymphopenia with lymphocytotoxins, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture=s syndrome, gout, Graves= disease, Hashimoto=s thyroiditis, hypereosinophilia, irritable bowel syndrome, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, psoriasis, Reiter=s syndrome, rheumatoid arthritis, scleroderma, Sj~Sgren=s syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, thrombocytopenic purpura, ulcerative colitis, uveitis, Wemer syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, viral, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma; a neurological disorder, such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer=s disease, Pick=s disease, Huntington's disease..... [and the lists goes on through the entirety of the next page]

At page 22, CADECM is defined as follows:

Various embodiments of the invention provide purified polypeptides, cell adhesion and extracellular matrix proteins, referred to collectively as >CADECM= and individually as >CADECM-1,= >CADECM-2,= >CADECM-3,= >CADECM-4,= >CADECM-5,= >CADECM-6,= >CADECM-7,= >CADECM-8,= >CADECM-9,= >CADECM-10,= >CADECM-11,= >CADECM-12,= >CADECM- 13,= >CADECM- 14,= >CADECM- 15,= >CADECM- 16,= >CADECM- 17,=>CADECM-18,= >CADECM-19,= >CADECM-20,= >CADECM-21 ,= >CADECM-22,=>CADECM-23,= >CADECM-24,= >CADECM-25,= >CADECM-26,= >CADECM-27,=>CADECM-28,= >CADECM-29,= >CADECM-30,= >CADECM-31,= >CADECM-32,=>CADECM-33,= >CADECM-34,= >CADECM-35,= >CADECM-36,= >CADECM-37,=>CADECM-38,= >CADECM-39,= >CADECM-40,= >CADECM-41,= and >CADECM-42' .....

Therefore, the list of diseases at page 62 is not specific to CADECM-11 comprising SEQ ID NO: 11, but rather a potential treatment of diseases by any one of 42 CADECMs. The only comment on the activity of SEQ ID NO: 11 is provided in Table 2 (at page 113 of that version of the specification), in which the annotation states that it is a human receptor of advanced glycosylation end products of proteins (RAGE).

As noted in the rejection, the prior art recognizes many splice variants of RAGE. The prior art recognizes that these splice variants have different functions, from being a RAGE decoy, an inhibitor of RAGE, and having less or different activity than RAGE, for example. Thus, prior art teachings submitted by Applicants does not address what this splice variant of RAGE does and cannot establish utility for this splice variant (having SEQ ID NO: 11).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 140, 144-146 and 157 are also again rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicants traverse this rejection on the same basis as they traversed the rejection of the claims under 35 USC 101. See the Examiner's response above.

Claims 157 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In Claim 157, no activity is associated with polynucleotides having at least 90% identity to SEQ ID NO: 53. Thus, claim 157 lacks written description. Evidence of possession of these variants include:

Level of skill in the art: The art does not recognize any activity associated with a polypeptide encoded by this fragment or variant.

Complete or partial structure: No activity is associated with the complete or partial structure.

Physical and/or chemical properties: No physical or chemical properties are provided.

Functional characteristics: there are no functional characteristics provided in the specification for the variant or fragment.

Correlation between structure and function: There is no function correlated with structure set forth in the specification.

Method of making the variants: is well-known in the art, but not with respect to assaying the function of the variant.

Applicants urge that one skilled in the art would understand that a polynucleotide having at least 90% identity to SEQ ID NO: 53 would encode a protein that has the same activity as one encoded by SEQ ID NO: 53.

As noted in the rejection of the claims under 35 USC 101, no activity has been assigned to SEQ ID NO: 11, which is encoded by SEQ ID NO: 53. Additionally, a splice variant of RAGE may

be an antagonist of RAGE as taught by Schlueter et al., for example. Thus, one skilled in the art cannot know that a polynucleotide having at least 90% identity would encode a protein having the same activity as SEQ ID NO: 11 because the activity of SEQ ID NO: 11 is unknown.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen Cochrane Carlson PhD

***

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER